January 25, 1950.

Dr. A. J. Weil,
Bronx Hospital,
New York 56, N.Y.

Dear Dr. Weil:

I was very glad to read that you had considered, in some detail, that phage might mimic the action of a transforming principle. Had I known this, I would certainly have emphasized it, and enlarged my too brief reference to your interesting work in the review article.

The problem is partly one of definition, partly one of methodology. An attempt to correlate lysogenicity with phage might start with the question whether any given transforming principle is a phage in the sense that it will lyse some detector strain. A number of examples are known of "sensitive" bacteria which can be made lysogenic without any sign of lysis, at least under certain conditions. One may imagine a phage losing its lytic capacity for most, or finally all, of its potential sensitive hosts, and this might well constitute its transition to a "pure" transforming principle. In the review, I hoped to point out the need for investigating this correlation, because I have the impression that lysogenicity is one of the forgotten phenomena of bacteriology. In my own experience, it is much more prevalent than I would have conceived possible, until I started looking for it. In fact, E. coli K-12 itself turns out to be lysogenic, but this does not appear to have anything to do with recombination. Except for the fortuitous isolation of a sensitive "mutant", we would not know to this day that it was lysogenic. Almost all of the Salmonella cultures, of various species, that we have examined, prove to be lysogenic, and for the rest we cannot be sure that we will not later turn up some indicator strain that will remove them from the "ultra-pure" category also.

I can offer no counter-arguments to your observations, except that one can never know whether some sensitive bacterial strain may sometime be isolated on which the lytic action of the "phage" will be demonstrable. The burden of proof is clearly in the other direction, but I think there may be some illustrative examples where a phage may mimic a transforming principle. (E.G., K-12, in which the lysogenic phage interferes with certain other phages, i.e., where a "transformation for phage-resistance" is possible.) Lysogenicity might mimic transformation either by 1) selection of resistant mutants, or 2) more strictly, the phage itself acting as the transferred hereditary particle, with possible incident effects on the other characters of the bacterium.

Sincerely,

Joshua Lederberg